REMARKS

Claims 1-49 and 53-54 were previously cancelled without prejudice. Claim 61 has been withdrawn. Applicants reserve the right to file divisional applications directed to the withdrawn subject matter. Claim 56 has been amended to correct typographical errors. No new matter has been added. Claims 50-52, 55-60 and 62 are currently pending.

Claim Objection

Claim 56 has been objected to because of typographical errors. Claim 56 has been amended to correct the errors. Withdrawal of the objection is respectfully requested.

Rejection Under 35 U.S.C. §102(e)

Claims 50-52 and 55-60 have been rejected under 35 U.S.C. §102(e) as anticipated by Tsuji *et al.* (U.S. Patent Application No. 2003/0157135; hereinafter "Tsuji"). The Examiner states that Tsuji teaches the administration of galactosylceramide to modulate the immune response in a mammal. See Office Action at page 3. The Examiner also states that, because of its immunostimulatory nature, the administration of galactosylceramide would necessarily modulate the immune response in an individual regardless of the type of disease. See Office Action at page 3-4.

Applicants respectfully traverse the rejection. To support a rejection under Section 102, an Examiner must show that each and every element recited in the claimed invention is taught by a single reference. MPEP §2131. In addition, to constitute an anticipatory reference, the prior art must contain an enabling disclosure. *Chester v. Miller*, 906 F.2d 1574, 1576 (Fed. Cir. 1990). A reference is not enabling if it does not disclose an operable technique to produce the product or perform the process disclosed by the reference. *In re Sasse*, 629 F.2d 675, 681 (CCPA 1980).

Tsuji relates to methods and compositions for augmenting the immunogenicity of an antigen in a mammal comprising administering the antigen together with an adjuvant. The adjuvant comprises glycosylceramide. The glucosylceramide is represented by the general Formula I (paragraph [0034]). This diagram indicates an alpha linkage. Tsuji therefore teaches an alpha glycosylceramide regardless of the sugar or ceramide included in the composition. One of ordinary skill in the art would understand that alpha glycosylceramides are not mammalian metabolites or intermediary metabolites. The composition taught and

disclosed in Tsuji is not a mammalian intermediary metabolite.

In contrast, the present invention relates to a process for regulating and manipulating immune responses in *mammalian* subjects by manipulating the levels of intermediary metabolites. This is accomplished by administering to the subject an effective amount of a *mammalian* intermediary metabolite. The specification defines metabolites or intermediary metabolites as "products of enzymatic processes in a mammalian system." Specification at page 7, line 22-23.

As explained above, an alpha glycosylceramide is not a mammalian intermediary metabolite. A beta-glycolipid is a normal constituent of mammalian cells whereas an alpha-glycolipid is recognized as "foreign" by the mammalian system. Applicants have found that a normal mammalian metabolite (*i.e.*, a beta-glycolipid) is able to alter the immune state. This is a surprising and unexpected result. Therefore, the compound taught by Tsuji is not a mammalian intermediary metabolite, as defined and required by the present claims, because the Tsuji composition is an alpha-glycolipid. Thus, Tsuji does not teach each and every element of the current claims. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claims 50 and 62 are rejected under 35 U.S.C. §103(a) as being obvious over Tsuji. The Examiner states that although Tsuji does not teach the administration of galactocylceramide to a human, such treatment is suggested by the reference. The Examiner then concludes that it would have been *prima facie* obvious to administer galactocylceramide to a human because the immunostimulatory activity of galactocylceramide is known in the art. Applicants respectfully disagree with the rejection.

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness. If the Examiner does not satisfy this burden, then the Applicant is not obligated to submit evidence of non-obviousness. See M.P.E.P § 2142 at 2100-133 (8th ed., incorporating Revision No. 5, August 2006). The recently revised Examiner guidelines for assessing obviousness set forth detailed requirements based on asserted rationales for obviousness. The Rationales To Support Rejections Under 35 U.S.C. § 103 provide the following possible rationales:

> (A) Combining prior art elements according to known methods to yield predictable results;

> (B) Simple substitution of one known element for another to obtain predictable results;
>
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
>
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
>
> (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
>
> (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
>
> (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

See MPEP 8th Edition, rev. 6, § 2141.

Applicant understands this rejection to conform to rationale G quoted above. The MPEP further sets forth the requirements for an obviousness rejection under this rationale:

> To reject a claim based on [rationale G], Office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:
>
> (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
>
> (2) a finding that there was reasonable expectation of success; and
>
> (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.
>
> The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success." DyStar Textilfarben GmbH & Co.

> Deutschland KG v. C.H. Patrick Co., 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006). **If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.**

See MPEP 8th Edition, rev 6, §2143

For at least the following reason, the Examiner has not shown that claims 50 and 62 are obvious over Tsuji.

The reference does not render the claims obvious because a person of ordinary skill in the art would have no motivation to alter the reference and no reasonable expectation of success when altering the reference. The compound of Tsuji is used to augment the immunogeneicty of an antigen. As such, the Tsuji composition is used as an adjuvant composition. The antigen *must* be combined with an adjuvant. See Abstract; paragraph [0034] (...comprising administering said antigen cojointly with an adjuvant composition."); paragraph [0069] ("...cojoint administration is used to refer to administration of an immune adjuvant and an antigen simultaneously in one composition..."). The adjuvant composition augments or increases the effectiveness of the antigen.

In contrast, the present invention relates to a process for regulating and manipulating immune responses in mammalian subjects by manipulating the levels of intermediary metabolites. This is accomplished by administering to the subject an effective amount of a mammalian intermediary metabolite. The present method is performed through the use of a *single* composition (the intermediary metabolite). The intermediary metabolite is not used to augment the immunogenicity of the antigen. Rather, the intermediary metabolite by itself modulates a component of the immune system.

The Examiner states that it would have been obvious to administer galactocylceramide to a human because the immunostimulatory activity of galactocylceramide is known in the art. As the Examiner correctly acknowledges, one of the requirements for a *prima facie* finding of obviousness is a reasonable expectation of success. However, a reasonable expectation of success requires more than the mere technical ability to carry out the steps of the claimed process. As provided in the MPEP:

> **2143.02 Reasonable Expectation of Success Is Required**

> A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art.

See MPEP 8th ed., rev. 6, § 2143.02.

Thus, the mere fact that two compounds have similar activities is insufficient to establish a reasonable expectation of success. Rather, to establish a reasonable expectation of success, the Examiner must also show that "the combination would have yielded nothing more than predictable results to one of ordinary skill in the art." *Id.* At the time of Applicants' invention it was not known this normal constituent of mammalian cells (beta-glycolipid) was able to alter the immune state. Thus, whether the two compounds have the same general activity is irrelevant because prior to Applicants' disclosure there was no reasonable expectation that beta-glycolipid was able to alter the immune state. Absent a showing that there is a reasonable expectation of success, the claims are not *prima facie* obvious.

It is clear then that Tsuji in fact teaches away from the present invention as described above. Tsuji teaches the co-administration of two separate compounds, in contrast Applicants' single-component compound. In addition, the composition disclosed by Tsuji (an alpha-glycolipid) is *not* a mammalian metabolite (or a mammalian intermediary metabolite) as defined in the specification or required by the present claims. Therefore, no motivation exists to use the two-component composition taught in Tsuji to alter the metabolite levels in mammals. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to his counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,
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